

Duodenal microbiota in stunted undernourished children with enteropathy

Research snapshot¹

The link between environmental enteric dysfunction (EED), a disorder of the small intestine, and childhood under-nutrition has been theorised for many years. However, evidence of its contribution to growth outcomes has been limited due to the challenges of sampling small intestinal mucosa and microbiota. This study explored the link between the two by collecting plasma and duodenal samples of 110 stunted children (mean age 18 months; total samples collected included 4,077 plasma proteins and 2,619 duodenal proteins) living in an urban slum in Dhaka, Bangladesh, who had biopsy-confirmed EED. In addition, 21

plasma and 27 faecal samples from age-matched healthy children living in the same area were collected. Young, germ-free mice fed a Bangladeshi diet were subsequently colonised with bacterial strains cultured from the duodenal samples.

Results of the study indicated that, of the bacterial strains obtained from the children with EED, the absolute levels of a shared group of 14 duodenal bacterial taxa (which are not usually classified as enteropathogens) were negatively correlated with linear growth ($p=0.003$) and positively correlated with duodenal proteins linked to immune-inflammatory responses. When com-

paring these faecal microbiota to samples from healthy children, the representation of these 14 taxa was significantly different ($p<0.001$). When mice were colonised with the cultured duodenal strains from the children with EED, they developed enteropathy of the small intestine. Further studies are needed to determine whether findings can be generalised to other contexts.

These results indicate a causal relationship between stunting and enteropathy; particularly highlighting the role of 14 duodenal bacterial taxa. Exploring the mechanisms by which the small intestinal microbiota affect linear growth mediators in young children may help provide new therapeutic approaches to reduce and prevent stunting.

¹ Chen, R. Y. et al. 2020. Duodenal Microbiota in Stunted Undernourished Children with Enteropathy. *New Engl. J. Med.* 383; 4. DOI: 10.1056/NEJMoa1916004 <https://www.nejm.org/doi/full/10.1056/NEJMoa1916004>

Early childhood linear growth failure in low- and middle-income countries

Research snapshot¹

Stunting affects approximately 149 million children under five years old globally.² However, estimates rely on cross-sectional surveys, which offer only limited information on growth failure trajectory, persistence and timing of onset. Such survey data also masks the dynamics of linear growth and potential reversal of linear growth failure. Information on the age of onset and its persistence offers insights on when and how to intervene with preventative measures. In this study the authors analysed 31 longitudinal cohorts from 15 low- and middle-income countries in South Asia, sub-Saharan Africa and Latin America (62,993 children, aged 0-24 months) to estimate age-specific incidence and prevalence of stunting, linear growth velocity and reversal of linear growth failure.

Across cohorts, 12% of children were stunted at birth and 17% experienced incident stunting onset between birth and three months of age. Stunted children between birth and three months accounted for 40% of all children who experienced stunting by age 24 months. Between 0 and 15 months of age, less than 5% of children reversed their stunting status per month. In children who were able to reverse stunting, relapse was common. Overall, improvements to length-for-age z-scores among children who had shown stunting reversal were neither sustained nor large enough to eliminate linear growth deficits.

These findings highlight the importance of preventive interventions; particularly in the prenatal

and postnatal stage. Interventions to improve maternal nutrition, reduce adolescent pregnancies and reduce prenatal infections may reduce the risk of linear growth failure. Additionally, more focus should be placed on postnatal interventions. However, interventions to improve exclusive breastfeeding rates and complementary feeding practices have to date shown only limited impact on child linear growth and a paucity of effective postnatal interventions to improve stunting rates remains. The authors conclude that actions to identify alternative interventions (potentially multisector in nature) and improve the quality of current interventions within the first 1,000 days of life are essential.

¹ Benjamin-Chung, J., et al. (2020). Early childhood linear growth failure in low- and middle-income countries. medRxiv: 2020.2006.2009.20127001. www.medrxiv.org/content/10.1101/2020.06.09.20127001v1

² Based on old estimates, from World Health Organization Joint child malnutrition estimates – Levels and trends (2019 edition). [www.who.int/nutgrowthdb/estimates2018/en/\(2019\)](http://www.who.int/nutgrowthdb/estimates2018/en/(2019)). More recent estimates are available in the 2020 edition (144 million children globally are stunted).

Development of complementary foods for moderately wasted children to improve gut microbiota status

Research snapshot¹

Children with acute malnutrition have impaired development of gut microbiota, which can affect future growth and health. Current therapeutic foods used to treat acute malnutrition have not been formulated to improve impaired gut microbiomes. A recent comprehensive study integrated findings from pre-clinical animal models with small-scale human pilot studies to understand which microbial targets are associated with better growth and which ingredients in complementary foods could increase the representation and expressed beneficial functions of these growth-promoting microbes.

The use of serially collected plasma and faecal samples from severely wasted children in Bangladesh as they recovered, combined with anthropometric data and data from healthy children, allowed for identification of growth-promoting bacterial taxa. Animal models were then used to recreate healthy and impaired gut environments and study their response to various food ingredients, leading to the creation of microbiota-directed complementary food (MDCF) prototypes. Sixty-three children aged 12 to 18 months with moderate wasting were then recruited into a randomised, double-blind study of standard

treatment versus four promising MDCF prototypes. Analysis of plasma and faecal samples from these children identified which of the MDCFs was most effective at increasing presence of proteins associated with growth, bone formation, neuro-development and immune function, and improving gut microbiota to better resemble healthy children.

This promising start now requires the further investigation of this MDCF in larger studies and across different populations in order to assess its effectiveness in repairing gut microbiota in malnourished children and improving their subsequent growth and health. Innovations in this area have the potential to reduce relapse rates and minimise the long-term implications of acute malnutrition.

¹ Gehrig JL, Venkatesh S, Chang HW, et al. Effects of microbiota-directed foods in gnotobiotic animals and undernourished children. *Science*. 2019;365(6449): eaau4732. doi:10.1126/science.aau4732 <https://pubmed.ncbi.nlm.nih.gov/31296738/>